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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/533,935 | 05/04/2005 | Rubina Mian | GRT/3772-38 | 9653 |

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| EXAMINER | |
|---|---|
| WOOD, AMANDA P | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1657 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/533,935 | MIAN ET AL. | |
| | Examiner | Art Unit | |
| | Amanda P. Wood | 1657 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,5-14,16,17,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-14,16,17,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 May 2007 has been entered.

Claims 1-2, 5-14, 16-17, and 23-24 have been examined on the merits.

Applicant's arguments with respect to the 103 rejection of record of claims 1-2, 5-14, 16-17, and 23-24 have been considered but are moot in view of the new ground(s) of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Claim Rejections - 35 USC § 112*

Claims 1-2, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Based upon the amendments to claim 1 regarding part (c), further clarification is necessary to determine the meaning of the claims. In particular, part (c) of claim 1 is still unclear as to how the comparing step is being performed (i.e., superoxide production above basal observed in the test whole blood sample is being compared to superoxide production above basal observed

in the control whole blood sample, but it is unclear when a measurement was made for the basal test whole blood sample, to provide a second basal measurement, one for the test sample, and one for the control sample).

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

***Response to Arguments***

Applicant's arguments filed 31 May 2007 have been fully considered but they are not persuasive. The method steps provided in claim 1 seek to compare superoxide production above basal in a test sample with production above basal in a control sample, but the claimed method does not provide an actual step of measuring a basal superoxide production level in a control sample. The instant claim language merely alludes to the conditions under which such basal levels would be tested in a control sample, but does not provide actual method steps which measure a basal level in a control sample, whereas the instant claim does provide active steps for measuring a basal level in a test sample.

***Claim Rejections - 35 USC § 103***

Claims 1-5, 9-11, and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikawa et al (Can J Anaesth 1993) in view of Pfefferkorn (US 5,492,816).

A method is claimed for determining whether an individual is experiencing changed physiological status arising from exposure to a psychological stressor.

Mikawa et al beneficially teach a method wherein

Mikawa et al beneficially teach a method wherein a basal level of superoxide production, or control level, is measured in whole blood samples before anesthesia administration prior to a surgical procedure in infants and neonates. Mikawa et al beneficially teach methods wherein PMA and FMLP are used as inducers for production of superoxide in neutrophils. Mikawa et al further beneficially teach that after surgery, neonates had the greatest suppression of superoxide production by neutrophils, but infants also showed immunosuppression after surgery. Mikawa et al did suggest, however, that in the infant group, the decrease in superoxide production per unit of neutrophil could be compensated by an increased number of neutrophils in the peripheral blood. Mikawa et al beneficially teach that surgical stress, along with other factors, some of which include hormonal response, prostaglandins, and postoperative pain, can modulate immune system activity with respect to neutrophil response (see, for example, pg. 1164, col. 2; pg. 1165, col. 2; pg. 1167, and 1169).

Mikawa et al does not expressly teach a method wherein superoxide production is detected using luminol as an amplifier and the resulting chemiluminescence in measured.

Pfefferkorn beneficially teaches a method wherein luminol is used to measure the chemiluminescence in superoxide anion assays triggered by PMA or FMLP in cells such as polymorphonuclear nucleocytes (i.e., neutrophils). In particular, Pfefferkorn

beneficially teaches that inducers, in conjunction with luminol chemiluminescence assays for superoxide, are useful for enhancing detection of superoxide (see, Abstract, and col. 4, lines 15-35, and col. 3, lines 50-65).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Mikawa et al based upon the beneficial teachings provided by Pfefferkorn with respect to the art-recognized method of enhancing detection of superoxide anion using an amplifier, such as luminol, when using an inducer, such as FLMP or PMA, as discussed above. Furthermore, Mikawa et al particularly point out that neutrophil production of superoxide is depressed in infants and neonates undergoing surgery compared to basal levels in control samples taken prior to surgery, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Mikawa et al in conjunction with the methods of Pfefferkorn so as to determine whether an individual is experiencing a changed physiological status arising from exposure to a psychological stressor, such as a medical treatment (i.e., surgery) for the expected benefit of being able to positively identify such individuals and to provide a treatment to aid in recovery and fight off possible infection after surgery resulting from reduced neutrophil microbicidal activity. The result-effective adjustment of particular conventional working conditions (e.g., performing the test on a particular type of individual, e.g., mammals other than humans, or on birds) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Claims 1-2, 12-14, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikawa et al (Can J Anaesth 1993) in view of Carlson et al (US 6,319,953).

A method is claimed for determining whether an individual is experiencing changed physiological status arising from exposure to a psychological stressor, further comprising a method for screening a stress-relieving drug, and treating an individual suffering from stress.

Mikawa et al beneficially teach a method wherein a basal level of superoxide production, or control level, is measured in whole blood samples before anesthesia administration prior to a surgical procedure in infants and neonates. Mikawa et al beneficially teach methods wherein PMA and FMLP are used as inducers for production of superoxide in neutrophils. Mikawa et al further beneficially teach that after surgery, neonates had the greatest suppression of superoxide production by neutrophils, but infants also showed immunosuppression after surgery. Mikawa et al did suggest, however, that in the infant group, the decrease in superoxide production per unit of neutrophil could be compensated by an increased number of neutrophils in the

peripheral blood. Mikawa et al beneficially teach that surgical stress, along with other factors, some of which include hormonal response, prostaglandins, and postoperative pain, can modulate immune system activity with respect to neutrophil response (see, for example, pg. 1164, col. 2; pg. 1165, col. 2; pg. 1167, and 1169).

Mikawa et al do not expressly teach a method for screening stress-relieving drugs or treating individuals suffering from stress identified by the methods as taught by Mikawa et al.

Carlson et al beneficially teach a method of screening for a stress-relieving drug, wherein a test compound is administered to an individual and the individual is then exposed to a psychological stressor. Furthermore, Carlson et al beneficially teach that measurements are made to determine the effect of the stress on the individual, and then compared to the individual's own baseline or to other individuals of the same species which receive no test compound. Furthermore, Carlson et al particularly teach a method for treatment of stress (i.e., anxiety) which comprises administration to a patient in need (i.e., a patient suffering from stress) an amount of a compound that gives effective relief of said stress, as determined by the methods taught by Carlson et al (see, for example, Abstract, col. 36, lines 10-65, and col. 42, lines 15-67).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Mikawa et al based upon the beneficial teachings provided by Carlson et al with respect to the art-recognized method of screening for stress-relieving drugs and treating individuals suffering from stress by providing a stress-relieving treatment, as discussed above.

Furthermore, Mikawa et al particularly point out that neutrophil production of superoxide is depressed in infants and neonates undergoing surgery compared to basal levels in control samples taken prior to surgery, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Mikawa et al in conjunction with the methods of Carlson et al so as to determine whether an individual is experiencing a changed physiological status arising from exposure to a psychological stressor, such as a medical treatment (i.e., surgery) for the expected benefit of being able to provide a treatment to aid in recovery and fight off possible infection after surgery resulting from reduced neutrophil microbicidal activity. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made, provided with the teachings of Mikawa et al and Carlson et al, to synthesize a stress-relieving drug identified by the methods of Mikawa et al and Carlson et al, and to administer such a drug to individuals identified by the method of Mikawa et al and to further test the efficacy of such a drug using the methods provided by Carlson et al and Mikawa et al, so as to be able to properly identify individuals exposed to a stressor and treat them with a drug that will alleviate the stress-induced decrease in neutrophil response, which predisposes individuals to infections and other immunosuppressive effects.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of

ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW

CHRISTOPHER R. TATE
PRIMARY EXAMINER

APW
Art Unit 1657